WHAT IS CLAIMED IS:

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1. A compound of Formula I:

	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$
2	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$
3	·
4	or a pharmaceutically acceptable salt or prodrug thereof,
5	wherein:
6	R ¹ is a member selected from the group consisting of H, C ₆ -C ₁₀ aryl substituted with
7	0-3 R ^{1a} , a 5- to 6-membered monocyclic or 8- to 10-membered bicyclic
8	heteroaryl containing 1 to 4 heteroatoms each independently a member
9	selected from the group consisting of N, O and S, wherein said heteroaryl is
10	substituted with 0-3 R ^{1a} , a C ₃ -C ₈ cycloalkyl substituted with 0-2 R ^{1b} , wherein
11	said C ₃ -C ₈ cycloalkyl is saturated or unsaturated; and a C ₃ -C ₈ heterocycle
12	containing 1 to 2 heteroatoms each independently a member selected from the
13	group consisting of N, O and S, wherein said heterocycle is substituted with
14	0-2 R ^{1c} and is saturated or unsaturated;
15	each R ^{1a} is independently a member selected from the group consisting of H, C ₁ -C ₃
16	perfluoroalkyl, C ₃ -C ₇ cycloalkyl, F, Cl, Br, CN, NO ₂ , OR ¹⁰ , SCH ₃ , S(=O)CH ₃ ,
17	$S(=O)_2R^{10}$, $NR^{11}R^{12}$, acetyl, $C(=O)OR^{13}$, $C(=O)NR^{13}R^{14}$, $S(=O)_2NR^{13}R^{14}$,
18	phenyl substituted with 0-3 R ¹⁵ , a 5- to 6-membered monocyclic heteroaryl
19	containing 1 to 4 heteroatoms each independently a member selected from the
20	group consisting of N, O and S, wherein said heteroaryl is substituted with 0-2
21	R ¹⁵ , a C ₃ -C ₈ heterocycle containing 1 to 2 heteroatoms each independently a
22	member selected from the group consisting of N, O and S, wherein said
23	heterocycle is substituted with 0-2 R ^{1c} and is saturated or unsaturated, and a
24	C_1 - C_4 alkyl substituted with 0-2 R^{16} ;
25	each R ^{1b} is independently a member selected from the group consisting of H, OH, F,
26	Cl, acetyl, =0, C_1 - C_6 alkyl, C_1 - C_6 alkoxy, CF_3 and OCF_3 ;
27	each R ^{1c} is independently a member selected from the group consisting of H, OH, F,
28	Cl, =O, C_1 - C_6 alkyl substituted with 0-2 R^{16} , C_1 - C_6 alkoxy, CF_3 , OCF_3 ,
29	C(=O)R ¹⁰ , S(=O) ₂ R ¹⁰ , tBoc, Cbz; phenyl substituted with 0-3 R ¹⁵ ; a 5- to 6-
30	membered monocyclic heteroaryl containing 1 to 4 heteroatoms each

31	independently a member selected from the group consisting of N, O and S,
32	wherein said heteroaryl is substituted with 0-2 R ¹⁵ ;
33	R ² is a member selected from the group consisting of a phenyl substituted with 0-3
34	R ¹⁵ , a 5- to 6-membered monocyclic heteroaryl containing 1 to 4 heteroatoms
35	each independently a member selected from the group consisting of N, O and
36	S, wherein said heteroaryl is substituted with 0-2 R ¹⁵ , a C ₁ -C ₆ alkyl substituted
37	with 0-2 R ^{2a} , wherein said C ₁ -C ₆ alkyl optionally contains a heteroatom
38	selected from the group consisting of -O-, -S-, and -S(=O) ₂ -, a C ₂ -C ₆ alkenyl,
39	a C_2 - C_6 alkynyl, a C_3 - C_7 cycloalkyl substituted with 0-2 R^{19} , wherein said C_3 -
40 .	C ₇ cycloalkyl optionally contains a heteroatom selected from -O-, -S-, and -
41	$S(=O)_{2}$, and a C_7 - C_{11} bicycloalkyl substituted with 0-2 R^{19} ;
42	each R ^{2a} is independently a member selected from the group consisting of a C ₆ -C ₁₀
43	aryl substituted with 0-3 R ¹⁵ , a 5- to 6-membered monocyclic or 8- to 10-
44	membered bicyclic heteroaryl containing 1 to 4 heteroatoms each
45	independently a member selected from the group consisting of N, O and S,
46	wherein said heteroaryl is substituted with 0-3 R ¹⁵ , a C ₃ -C ₈ cycloalkyl
47	substituted with 0-2 R ¹⁹ , and a C ₇ -C ₁₁ bicycloalkyl substituted with 0-2 R ¹⁹ ;
48	R ³ is a member selected from the group consisting of H and C ₁ -C ₄ alkyl;
49	subscript n is 0 or 1;
50	R ⁴ is a member selected from the group consisting of H and C ₁ -C ₆ alkyl;
51	alternatively, R ² and R ⁴ are taken together to form a C ₅ -C ₇ cycloalkyl substituted with
52	0-2 R ¹⁹ ;
53	R ⁵ is a member selected from the group consisting of H, C ₃ -C ₇ cycloalkyl, C ₂ -C ₆
54	alkenyl, C ₂ -C ₆ alkyne, phenyl substituted with 0-2 R ¹⁵ ; 5- to 6-membered
55	heteroaryl containing 1 to 4 heteroatoms each independently a member
56	selected from the group consisting of N, O and S, wherein said heteroaryl is
57	substituted with 0-2 R ¹⁵ , a C ₁ -C ₆ alkyl substituted with 0-2 R ¹⁸ , wherein said
58	C ₁ -C ₆ alkyl optionally contains a heteroatom selected from the group
59	consisting of $-O$ -, $-S$ -, $-S(=O)$ -, $-S(=O)_2$ - and $-NR^{17}$ -;
60	Y is a member independently selected from the group consisting of a bond and
61	$-(CR^{20}R^{21})_{m}-W-(CR^{22}R^{23})_{p}-;$
62	subscript p is 1 or 2;
63	subscript m is 0 or 1;

64	W is a member independently selected from the group consisting of a bond, -O-, -S-,
65	$-S(=O)$ -, $-S(=O)_2$ - and $-NR^{12}$ -;
66	X is selected from the group consisting of -C(=O)-, -OC(=O)-, -NR ²⁴ C(=O)- and
67	-S(=O) ₂ -;
68	each of R ⁶ , R ⁷ , R ⁸ and R ⁹ is independently a member selected from the group
69	consisting of H and C ₁ -C ₄ alkyl;
70 ·	alternatively, R ⁵ and R ⁷ are taken together to form a C ₅ -C ₇ cycloalkyl substituted with
71	0-2 R ¹⁹ ;
72	alternatively, R ⁵ and R ⁹ are taken together to form a 6-7 membered heterocyclic ring
73	containing 1-2 heteroatoms each independently a member selected from the
74	group consisting of N, O and S;
75	Ar is a member selected from the group consisting of phenyl substituted with 0-3 R ²⁹ ,
76	and 5- to 6-membered heteroaryl containing 1 to 4 heteroatoms each
77	independently a member selected from the group consisting of N, O and S,
78	wherein said heteroaryl is substituted with 0-3 R ²⁹ ;
79	each R ¹⁰ is independently a member selected from the group consisting of H, C ₃ -C ₇
80	cycloalkyl, a C ₁ -C ₃ perfluoroalkyl, a C ₁ -C ₄ alkyl substituted with 0-1 R ²⁵ , a
81	phenyl substituted with 0-3 R ¹⁵ ; a 5- to 6-membered heteroaryl containing 1 to
82	4 heteroatoms each independently a member selected from the group
83 .	consisting of N, O and S, wherein said heteroaryl is substituted with 0-2 R ¹⁵ ,
84	and a C ₃ -C ₈ heterocycle containing 1 to 2 heteroatoms each independently a
85	member selected from the group consisting of N, O and S, wherein said
86	heterocycle is substituted with 0-2 R ^{1c} ;
87	each R ¹¹ is independently a member selected from the group consisting of H, 'BOC,
88	Cbz, C_3 - C_8 cycloalkyl, $(C_1$ - C_6 alkyl)- $C(=O)$ -, $(C_1$ - C_6 alkyl)- $S(=O)_2$ - and a
89	C_1 - C_6 alkyl;
90	each of R ¹² , R ¹³ and R ¹⁴ is independently a member selected from the group
91	consisting of H and C ₁ -C ₄ alkyl;
92	alternatively, R ¹³ and R ¹⁴ on the same N atom are taken together to form a C ₅ -C ₇
93	heterocycle containing 1-2 heteroatoms each independently a member selected
94	from the group consisting of N, O and S;
95	each R ¹⁵ is independently a member selected from the group consisting of H, OH, F,
96	Cl, Br, I, CN, NO ₂ , COOR ¹³ , C(=O)NR ¹³ R ¹⁴ , S(=O) ₂ NR ¹³ R ¹⁴ acetyl -SCH ₂

97	$-S(=O)CH_3$, $-S(=O)_2CH_3$, $NR^{26}R^{27}$, C_1-C_6 alkoxy, C_1-C_3 perfluoroalkyl, C_1-C_3
98	perfluoroalkoxy and a C ₁ -C ₆ alkyl;
99	each R ¹⁶ is independently a member selected from the group consisting of H, OH,
100	$COOR^{13}$, $C(=O)NR^{13}R^{14}$, $S(=O)_2NR^{13}R^{14}$, acetyl, -SCH ₃ , -S(=O)CH ₃ ,
101	-S(=O) ₂ CH ₃ , C ₁ -C ₆ alkoxy, NR ²⁶ R ²⁷ , a phenyl substituted with 0-3 R ¹⁵ , a 5- to
102	6-membered heteroaryl containing 1 to 4 heteroatoms each independently a
103	member selected from the group consisting of N, O and S, wherein said
104	heteroaryl is substituted with 0-3 R ¹⁵ , and a C ₃ -C ₈ heterocycle containing 1 to
105	2 heteroatoms each independently a member selected from the group
106	consisting of N, O and S, wherein said heterocycle is substituted with 0-2 R ¹⁵
107	and is saturated or unsaturated;
108	R ¹⁷ is a member selected from the group consisting of H and C ₁ -C ₄ alkyl;
109	each R ¹⁸ is independently a member selected from the group consisting of H, OH, F,
110	Cl, CN, NO ₂ , C(=O)OR ³⁰ , C(=O)NR ¹³ R ¹⁴ , NR ¹¹ R ¹² , a C ₁ -C ₃ perfluoroalkyl, a
111	C ₁ -C ₃ perfluoroalkoxy, a phenyl substituted with 0-3 R ¹⁵ , a 5- to 6-membered
112	heteroaryl containing 1 to 4 heteroatoms each independently a member
113	selected from the group consisting of N, O and S, wherein said heteroaryl is
114	substituted with 0-3 R ¹⁵ , a C ₃ -C ₈ heterocycle containing 1 to 2 heteroatoms
115	each independently a member selected from the group consisting of N, O and
116	S, wherein said heterocycle is substituted with 0-2 R ¹⁵ and is saturated or
117	unsaturated; and C ₃ -C ₈ cycloalkyl;
118	each R ¹⁹ is a independently a member selected from the group consisting of C ₁ -C ₄
119	alkyl, F, Cl and C ₁ -C ₄ alkoxy, CF ₃ and OCF ₃ ;
120	alternatively, two R ¹⁹ on the same carbon may be combined to form C ₃ -C ₆ cycloalkyl;
121	each of R ²⁰ , R ²¹ , R ²² and R ²³ is independently a member selected from the group
122	consisting of a bond, H, F, OH, C ₁ -C ₄ alkyl, and C ₁ -C ₃ alkylhydroxy;
123	alternatively, R^{20} and R^{21} or R^{22} and R^{23} are taken together to form a C_3 - C_6
124	cycloalkyl;
125	R ²⁴ is a member selected from the group consisting of H and C ₁ -C ₄ alkyl;
126	each R ²⁵ is independently a member selected from the group consisting of H, C ₃ -C ₇
127	cycloalkyl, a phenyl substituted with 0-3 R ¹⁵ and a 5- to 6-membered
128	heteroaryl containing 1 to 4 heteroatoms each independently a member
129	selected from the group consisting of N, O and S, wherein said 5- to 6-
130	membered heteroaryl is substituted with 0-2 R ¹⁵ ;

131	each R ²⁶ is independently a member selected from the group consisting of H, C ₁ -C ₄
132	alkyl, $(C_1-C_4 \text{ alkyl})-C(=O)$ - and $(C_1-C_4 \text{ alkyl})-S(=O)_2$ -;
133	each R ²⁷ is independently a member selected from the group consisting of H and
134	C_1 - C_4 alkyl;
135	alternatively, R ²⁶ and R ²⁷ on the same N atom are taken together to form a C ₅ -C ₇
136	heterocycle containing 1-2 heteroatoms each independently a member selected
137	from the group consisting of N, O and S;
138	each R ²⁸ is independently a member selected from the group consisting of H, a C ₁ -C ₆
139	alkyl, C ₃ -C ₈ cycloalkyl, a phenyl substituted with 0-3 R ¹⁵ , a benzyl
140	substituted with 0-2 R ¹⁵ ;
141	each R ²⁹ is independently a member selected from the group consisting of H, F, Cl,
142	Br, I, CN, NO ₂ , OR^{28} , SR^{28} , $S(=O)R^{28}$, $S(=O)_2R^{28}$, $S(=O)_2NR^{13}R^{14}$, $NR^{26}R^{27}$,
143	acetyl, C(=O)NR ¹³ R ¹⁴ , C(=O)OR ¹³ , C ₁ -C ₆ alkyl, OCHF ₂ , SCF ₃ , OCF ₃ , -
144	C(=NH)NH ₂ , and 5- to 6-membered heteroaryl containing 1 to 4 heteroatoms
145	each independently a member selected from the group consisting of N, O and
146	S;
147	alternatively, two R ²⁹ substituted on adjacent atoms may be combined to form a 5 to 6
148	membered heterocyclic fused radical, wherein said 5 to 6 membered
149	heterocyclic fused radical comprise 1 or 2 heteroatom(s) selected from O, S
150	and N; wherein said 5 to 6 membered heterocyclic fused radical is substituted
151	with 0-1 oxo;
152	alternatively, R ²⁹ and R ⁹ are taken together to form a 5- to 7-membered fused
153	heterocyclic ring containing 1-2 heteroatom(s) each independently a member
154	selected from the group consisting of N, O and S; wherein said 5 to 7
155	membered fused heterocyclic ring is substituted with 0-2 R ¹⁹ ;
156	each R ³⁰ is independently a member selected from the group consisting of H, C ₃ -C ₇
157	cycloalkyl, C ₁ -C ₄ alkyl substituted with 0-1 R ²⁵ , a phenyl substituted with 0-3
158	R ¹⁵ , and a 5- to 6-membered heteroaryl containing 1 to 4 heteroatoms each
159	independently a member selected from the group consisting of N, O and S,
160	wherein said heteroaryl is substituted with 0-3 R ¹⁵ ; and
161	with the proviso that R ³ , R ⁴ , R ⁵ , R ⁶ , R ⁷ , R ⁸ , and R ⁹ are not all hydrogen.

2. The compound of claim 1, according to formula Ia

Ia

4 wherein:

- R¹ is a 5- to 6-membered heteroaryl containing 1 to 4 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heteroaryl is substituted with 1 R^{1a};
- R^{1a} is independently a member selected from the group consisting of phenyl substituted with 0-2 R¹⁵, and a 5- to 6-membered monocyclic heteroaryl containing 1 to 4 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heteroaryl is substituted with 0-2 R¹⁵:
- R² is a member selected from the group consisting of a phenyl substituted with 0-3 R¹⁵, a 5- to 6-membered monocyclic heteroaryl containing 1 to 4 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heteroaryl is substituted with 0-2 R¹⁵, a C₁-C₆ alkyl, a C₁-C₃ alkyl substituted with 1 R^{2a}, and a C₃-C₇ cycloalkyl substituted with 0-2 R¹⁹;
- each R^{2a} is independently a member selected from the group consisting of a C_6 - C_{10} aryl substituted with 0-3 R^{15} , a 5- to 6-membered monocyclic or 8- to 10-membered bicyclic heteroaryl containing 1 to 4 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heteroaryl is substituted with 0-3 R^{15} , a C_3 - C_8 cycloalkyl substituted with 0-2 R^{19} ; and
- Ar is phenyl substituted with 0-3 R²⁹, or alternatively, R²⁹ and R⁹ are taken together to form a 5- to 7-membered fused heterocyclic ring containing 1-2 heteroatom(s) each independently a member selected from the group consisting of N, O and S; wherein said 5- to 7-membered fused heterocyclic ring is substituted with 0-2 R¹⁹.
 - 3. The compound of claim 2, wherein said compound is of the formula:

4. The compound of claim 1, wherein:

R¹ is a member selected from the group consisting of phenyl substituted with 0-3 R^{1a}, furanyl substituted with 0-3 R^{1a}, C₃-C₆ cycloalkyl substituted with 0-3 R^{1a}, indolyl substituted with 0-3 R^{1a}, 5- or 6-membered heterocyclyl substituted with 0-3 R^{1c}, pyidazinyl substituted with 0-3 R^{1a}, imadazolyl substituted with 0-3 R^{1a}, thienyl substituted with 0-3 R^{1a}, thiazolyl substituted with 0-3 R^{1a}, oxadiazolyl substituted with 0-3 R^{1a}, pyrazolyl substituted with 0-3 R^{1a}, isoxazolyl substituted with 0-3 R^{1a}, tetrazolyl substituted with 0-3 R^{1a}, oxazolyl substituted with 0-3 R^{1a} and pyridyl substituted with 0-3 R^{1a}.

5. The compound of claim 2, according to formula Ib:

Ib

wherein:

each R^{15} , if present, is independently a member selected from the group consisting of OH, F, Cl, Br, I, CN, NO₂, COOR¹³, C(=O)NR¹³R¹⁴, S(=O)₂NR¹³R¹⁴, acetyl, -SCH₃, -S(=O)CH₃, -S(=O)₂CH₃, NR²⁶R²⁷, C₁-C₆ alkoxy, C₁-C₃ perfluoroalkyl, C₁-C₃ perfluoroalkoxy and a C₁-C₆ alkyl; and

A is a 5-membered heteroaryl selected from the group consisting of furanylene, thienylene, thiazolylene, oxadiazolylene, isoxazolylene, tetrazolylene, and oxazolylene.

6. The compound of claim 5, wherein:

- R^2 is a member selected from the group consisting of a C_1 - C_2 alkyl substituted with 1 R^{2a} , and C_1 - C_6 alkyl;
- each R^{2a} is independently a member selected from the group consisting of a phenyl substituted with 0-3 R¹⁵, and a C₃-C₈ cycloalkyl substituted with 0-2 R¹⁹;
- R^5 is a member selected from the group consisting of H, C_3 - C_7 cycloalkyl; a C_1 - C_6 alkyl substituted with 0-1 R^{18} , wherein said C_1 - C_6 alkyl optionally contains a heteroatom selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)_2- and -NR¹⁷-; and

each R¹⁸ is independently a member selected from the group consisting of H, OH, F, Cl, CN, C(=O)OR³⁰, C(=O)NR¹³R¹⁴, NR¹¹R¹², a phenyl substituted with 0-3 R¹⁵, a C₃-C₈ heterocycle containing 1 to 2 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heterocycle is substituted with 0-2 R¹⁵ and is saturated or unsaturated; and C₃-C₈ cycloalkyl.

7. The compound of claim 1, according to formula Ia:

34 wherein:

R¹ is a member selected from the group consisting of a C₃-C₈ cycloalkyl substituted with 0-2 R^{1b}, wherein said C₃-C₈ cycloalkyl is saturated or unsaturated and a C₄-C₇ heterocycle containing 1 to 2 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heterocycle is substituted with 0-2 R^{1c} and is saturated or unsaturated;

Ia

 R^2 is a member selected from the group consisting of a phenyl substituted with 0-3 R^{15} , a 5- to 6-membered monocyclic heteroaryl containing 1 to 4 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heteroaryl is substituted with 0-2 R^{15} , a C_1 - C_6 alkyl substituted with 0-2 R^{2a} , and a C_3 - C_7 cycloalkyl substituted with 0-2 R^{19} ; and

Ar is phenyl substituted with 0-3 R²⁹, or alternatively, R²⁹ and R⁹ are taken together to form a 5- to 7-membered fused heterocyclic ring containing 1-2 heteroatom(s) each independently a member selected from the group consisting of N, O and S; wherein said 5- to 7-membered fused heterocyclic ring is substituted with 0-2 R¹⁹.

8. The compound of claim 7, wherein:

- R^2 is a member selected from the group consisting of a C_1 - C_2 alkyl substituted with 1 R^{2a} , and C_1 - C_6 alkyl;
- each R^{2a} is independently a member selected from the group consisting of a phenyl substituted with 0-3 R¹⁵, and a C₃-C₈ cycloalkyl substituted with 0-2 R¹⁹;

- R⁵ is a member selected from the group consisting of H, C₃-C₇ cycloalkyl; a C₁-C₆ alkyl substituted with 0-1 R¹⁸, wherein said C₁-C₆ alkyl optionally contains a heteroatom selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)₂- and -NR¹⁷-; and
 - each R¹⁸ is independently a member selected from the group consisting of H, OH, F, Cl, CN, C(=O)OR³⁰, C(=O)NR¹³R¹⁴, NR¹¹R¹², a phenyl substituted with 0-3 R¹⁵, a C₃-C₈ heterocycle containing 1 to 2 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heterocycle is substituted with 0-2 R¹⁵ and is saturated or unsaturated; and C₃-C₈ cycloalkyl.
 - 9. The compound of claim 7, wherein said compound is of the formula:

10. The compound of claim 1, according to formula Ic:

3 . Ic

wherein:

- R¹ is a member selected from the group consisting of tBu, phenyl substituted with 0-2 R¹⁵, a 5- to 6-membered heteroaryl containing 1 to 4 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heteroaryl is substituted with 0-2 R¹⁵, and a C₄-C₇ heterocycle containing 1 to 2 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heterocycle is substituted with 0-2 R^{1c};
- each R^{1c} is independently a member selected from the group consisting of H, OH, F, Cl, =O, C₁-C₆ alkyl substituted with 0-2 R¹⁶, a C₁-C₆ alkoxy, CF₃, OCF₃, C(=O)R¹⁰, S(=O)₂R¹⁰, tBoc, Cbz, phenyl substituted with 0-3 R¹⁵, and a 5- to 6-membered monocyclic heteroaryl containing 1 to 4 heteroatoms each

16	independently a member selected from the group consisting of N, O and S,
17	wherein said heteroaryl is substituted with 0-2 R ¹⁵ ;
18	Y is a member independently selected from the group consisting of a bond and
19	- $(CR^{20}R^{21})_m$ -W- $(CR^{22}R^{23})_p$ -, wherein m is 0, W is a bond, and $R^{22}R^{23}$ are both
20	Н;
21	R ² is a member selected from the group consisting of a phenyl substituted with 0-3
22	R ¹⁵ , a 5- to 6-membered monocyclic heteroaryl containing 1 to 4 heteroatoms
23	each independently a member selected from the group consisting of N, O and
24	S, wherein said heteroaryl is substituted with 0-2 R^{15} , a C_1 - C_6 alkyl, a C_1 - C_3
25	alkyl substituted with 1 R^{2a} , and a C_3 - C_7 cycloalkyl substituted with 0-2 R^{19} ;
26	each R^{2a} is independently a member selected from the group consisting of a C_6 - C_{10}
27	aryl substituted with 0-3 R ¹⁵ , a 5- to 6-membered monocyclic or 8- to 10-
28	membered bicyclic heteroaryl containing 1 to 4 heteroatoms each
29	independently a member selected from the group consisting of N, O and S,
30	wherein said heteroaryl is substituted with 0-3 R ¹⁵ , a C ₃ -C ₈ cycloalkyl
31	substituted with 0-2 R ¹⁹ , and a C ₇ -C ₁₁ bicycloalkyl substituted with 0-2 R ¹⁹ ;
32	and
33	Ar is phenyl substituted with 0-3 R ²⁹ , or alternatively, R ²⁹ and R ⁹ are taken together to
34	form a 5- to 7-membered fused heterocyclic ring containing 1-2 heteroatom(s)
35	each independently a member selected from the group consisting of N, O and
36	S; wherein said 5- to 7-membered fused heterocyclic ring is substituted with 0-
37	2 R ¹⁹ .
1	11. The compound of claim 10, wherein:
2	11. The compound of claim 10, wherein: R ² is a member selected from the group consisting of a C ₁ -C ₂ alkyl substituted with 1
3	R^{2a} , and C_1 - C_6 alkyl;
4	each R ^{2a} is independently a member selected from the group consisting of a phenyl
5	substituted with 0-3 R^{15} , and a C_3 - C_8 cycloalkyl substituted with 0-2 R^{19} ;
6	R ⁵ is a member selected from the group consisting of H, C ₃ -C ₇ cycloalkyl; a C ₁ -C ₆
7	alkyl substituted with 0-1 R^{18} , wherein said C_1 - C_6 alkyl optionally contains a
8	heteroatom selected from the group consisting of $-O$ -, $-S$ -, $-S(=O)$ -, $-S(=O)$ ₂ -
9	and $-NR^{17}$ -; and
10	each R ¹⁸ is independently a member selected from the group consisting of H, OH, F,
11	Cl, CN, C(=O)OR ³⁰ , C(=O)NR ¹³ R ¹⁴ , NR ¹¹ R ¹² , a phenyl substituted with 0-3
- -	or, or, or open to the R, a phony substituted with 0-3

12 R¹⁵, a C₃-C₈ heterocycle containing 1 to 2 heteroatoms each independently a
13 member selected from the group consisting of N, O and S, wherein said
14 heterocycle is substituted with 0-2 R¹⁵ and is saturated or unsaturated; and C₃15 C₈ cycloalkyl.

12. The compound of claim 10, wherein said compound is of the formula:

13. The compound of claim 1, according to formula Id:

3 Id

wherein:

- R¹ is a member selected from the group consisting of methyl, benzyl, C₆-C₁₀ aryl substituted with 0-3 R^{1a}, and a 5- to 6-membered monocyclic or 8- to 10-membered bicyclic heteroaryl containing 1 to 4 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heteroaryl is substituted with 0-3 R^{1a}:
- each R^{1a} is independently a member selected from the group consisting of H, C_1 - C_3 perfluoroalkyl, C_3 - C_7 cycloalkyl, F, Cl, Br, CN, NO₂, OR^{10} , SCH_3 , $S(=O)CH_3$, $S(=O)_2R^{10}$, $NR^{11}R^{12}$, acetyl, $C(=O)OR^{13}$, $C(=O)NR^{13}R^{14}$, $S(=O)_2NR^{13}R^{14}$, phenyl substituted with 0-3 R^{15} , a 5- to 6-membered monocyclic heteroaryl containing 1 to 4 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heteroaryl is substituted with 0-2 R^{15} ; and a C_1 - C_4 alkyl; and
- Ar is phenyl substituted with 0-3 R²⁹, or alternatively, R²⁹ and R⁹ are taken together to form a 5- to 7-membered fused heterocyclic ring containing 1-2 heteroatom(s) each independently a member selected from the group consisting of N, O and S; wherein said 5- to 7-membered fused heterocyclic ring is substituted with 0-2 R¹⁹.

- R^2 is a member selected from the group consisting of a C_1 - C_2 alkyl substituted with 1 R^{2a} , and C_1 - C_6 alkyl;
 - each R^{2a} is independently a member selected from the group consisting of a phenyl substituted with 0-3 R¹⁵, and a C₃-C₈ cycloalkyl substituted with 0-2 R¹⁹;
 - R^5 is a member selected from the group consisting of H, C_3 - C_7 cycloalkyl; a C_1 - C_6 alkyl substituted with 0-1 R^{18} , wherein said C_1 - C_6 alkyl optionally contains a heteroatom selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)₂- and -NR¹⁷-; and
 - each R¹⁸ is independently a member selected from the group consisting of H, OH, F, Cl, CN, C(=O)OR³⁰, C(=O)NR¹³R¹⁴, NR¹¹R¹², a phenyl substituted with 0-3 R¹⁵, a C₃-C₈ heterocycle containing 1 to 2 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heterocycle is substituted with 0-2 R¹⁵ and is saturated or unsaturated; and C₃-C₈ cycloalkyl.
 - 15. The compound of claim 13, wherein said compound is of the formula:

16. The compound of claim 1, according to formula Ie

3 Ie

wherein:

- R¹ is a member selected from the group consisting of a C₆-C₁₀ aryl substituted with 0-3 R^{1a}, a 5- to 6-membered monocyclic or 8- to 10-membered bicyclic heteroaryl containing 1 to 4 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heteroaryl is substituted with 0-3 R^{1a};
- each R^{1a} is independently a member selected from the group consisting of H, C₁-C₃ perfluoroalkyl, C₃-C₇ cycloalkyl, F, Cl, Br, CN, NO₂, OR¹⁰, SCH₃, S(=O)CH₃,

S(=O)₂R¹⁰, NR¹¹R¹², acetyl, C(=O)OR¹³, C(=O)NR¹³R¹⁴, S(=O)₂NR¹³R¹⁴, phenyl substituted with 0-3 R¹⁵, a 5- to 6-membered monocyclic heteroaryl containing 1 to 4 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heteroaryl is substituted with 0-2 R¹⁵, a C₃-C₈ heterocycle containing 1 to 2 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heterocycle is substituted with 0-2 R^{1c} and is saturated or unsaturated, and a C₁-C₄ alkyl substituted with 0-2 R¹⁶; and

Ar is phenyl substituted with 0-3 R²⁹, or alternatively, R²⁹ and R⁹ are taken together to form a 5- to 7-membered fused heterocyclic ring containing 1-2 heteroatom(s) each independently a member selected from the group consisting of N, O and S; wherein said 5- to 7-membered fused heterocyclic ring is substituted with 0-2 R¹⁹.

17. The compound of claim 16, wherein:

 R^2 is a member selected from the group consisting of a C_1 - C_2 alkyl substituted with 1 R^{2a} , and C_1 - C_6 alkyl;

each R^{2a} is independently a member selected from the group consisting of a phenyl substituted with 0-3 R¹⁵, and a C₃-C₈ cycloalkyl substituted with 0-2 R¹⁹; and R⁵ is a member selected from the group consisting of H, C₃-C₇ cycloalkyl; a C₁-C₆

alkyl, wherein said C_1 - C_6 alkyl optionally contains a heteroatom selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)₂- and $-NR^{17}$ -.

18. The compound of claim 16, wherein said compound is of the formula:

$$R^{1}\text{-}CHR^{23} - \overset{O}{C} - \overset{H}{N} - \overset{R^{2}}{C} - \overset{H}{N} - \overset{H}{C} - \overset{H}{C} - \overset{H}{C} - \overset{H}{N} - \overset{H}{C} - \overset{H}{C} - \overset{H}{N} -$$

19. The compound of claim 1, according to formula Ia

3 Ia

4 wherein:

R¹ is a member selected from the group consisting of C₆-C₁₀ aryl substituted with 0-3 R^{1a}, and a 5- to 6-membered monocyclic or 8- to 10-membered bicyclic heteroaryl containing 1 to 4 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heteroaryl is substituted with 0-3 R^{1a};

- each R^{1a} is independently a member selected from the group consisting of H, C_1 - C_3 perfluoroalkyl, C_3 - C_7 cycloalkyl, F, Cl, Br, CN, NO₂, OR¹⁰, SCH₃, S(=O)CH₃, S(=O)₂R¹⁰, NR¹¹R¹², acetyl, C(=O)OR¹³, C(=O)NR¹³R¹⁴, S(=O)₂NR¹³R¹⁴, phenyl substituted with 0-3 R¹⁵; and a C_1 - C_4 alkyl substituted with 0-2 R¹⁶:
- R² is a member selected from the group consisting of a phenyl substituted with 0-3 R¹⁵; a 5- to 6-membered monocyclic heteroaryl containing 1 to 4 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heteroaryl is substituted with 0-2 R¹⁵, a C₁-C₆ alkyl, a C₁-C₂ alkyl substituted with 1R^{2a}, a C₃-C₇ cycloalkyl substituted with 0-2 R¹⁹;
- each R^{2a} is independently a member selected from the group consisting of a C₆-C₁₀ aryl substituted with 0-3 R¹⁵; a 5- to 6-membered monocyclic or 8- to 10-membered bicyclic heteroaryl containing 1 to 4 heteroatoms each independently a member selected from the group consisting of N, O and S, wherein said heteroaryl is substituted with 0-3 R¹⁵; a C₃-C₈ cycloalkyl substituted with 0-2 R¹⁹; and a C₇-C₁₁ bicycloalkyl substituted with 0-2 R¹⁹; and
- Ar is phenyl substituted with 0-3 R²⁹, or alternatively, R²⁹ and R⁹ are taken together to form a 5- to 7-membered fused heterocyclic ring containing 1-2 heteroatom(s) each independently a member selected from the group consisting of N, O and S; wherein said 5- to 7-membered fused heterocyclic ring is substituted with 0-2 R¹⁹.
 - 20. The compound of claim 19, wherein said compound is of the formula:

1 21. The compound of claim 1, wherein R⁵ and R⁷ are taken together to 2 form a C₅-C₇ cycloalkyl substituted with 0-2 R¹⁹; and Ar is phenyl substituted with 0-3 R²⁹, or alternatively, R²⁹ and R⁹ are taken together to form a 5- to 7-membered fused heterocyclic ring containing 1-2 heteroatom(s) each independently a member selected from the group consisting of N, O and S; wherein said 5- to 7-membered fused heterocyclic ring is substituted with 0-2 R¹⁹.

22. The compound of claim 1, according to formula If

3 If

4 wherein:

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6 7

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1

2

Y is a member selected from the group consisting of a bond and -

$$(CR^{20}R^{21})_{m}$$
-W- $(CR^{22}R^{23})_{p}$ -;

subscript p is the integer 1 or 2;

subscript m is 0 or 1;

9 W is a oxygen; and

Ar is phenyl substituted with 0-3 R²⁹, or alternatively, R²⁹ and R⁹ are taken together to form a 5- to 7-membered fused heterocyclic ring containing 1-2 heteroatom(s) each independently a member selected from the group consisting of N, O and S; wherein said 5- to 7-membered fused heterocyclic ring is substituted with 0-2 R¹⁹.

23. The compound of claim 1, according to formula Ig:

$$R^{1}-Y-X-N-\overset{H}{\overset{R^{2}}{\overset{}_{U}}}\overset{H}{\overset{H}}\overset{H}{\overset{H}}\overset{H}{\overset{H}}\overset{H}{\overset{H}}\overset{H}{\overset{}_{U}}\overset{(R^{19})_{0-2}}{\overset{}_{U}}\overset{R^{29}}{\overset{}_{U}}$$

3 **Ig**

4 wherein:

R⁵ is a member selected from the group consisting of H, C₃-C₇ cycloalkyl, C₂-C₆
alkenyl, C₂-C₆ alkyne, phenyl substituted with 0-2 R¹⁵; 5- to 6-membered
heteroaryl containing 1 to 4 heteroatoms each independently a member
selected from the group consisting of N, O and S, wherein said heteroaryl is
substituted with 0-2 R¹⁵, a C₁-C₆ alkyl substituted with 0-2 R¹⁸, wherein said

- 10 C_1 - C_6 alkyl optionally contains a heteroatom selected from the group 11 consisting of -O-, -S-, -S(=O)-, -S(=O)₂- and -NR¹⁷-.
- 12
- 24. The compound of claim 23, according to formula Ih:

3

- 1 25. The compound of claim 1, wherein R⁹ is H; and
- 2 Ar is phenyl substituted with 0-3 R²⁹, or alternatively, R²⁹ and R⁹ are taken
- 3 together to form a 5- to 7-membered fused heterocyclic ring containing 1-2 heteroatom(s)
- 4 each independently a member selected from the group consisting of N, O and S; wherein said

Ih

I

- 5 5- to 7-membered fused heterocyclic ring is substituted with 0-2 R¹⁹.
- 1 **26**. The compound of claim 1, wherein said compound is a member 2 selected from the compounds of Table I.
- 1 27. A pharmaceutical composition comprising: a compound of Formula I:

2

4

or a pharmaceutically acceptable salt or prodrug thereof,

5 wherein:

- R¹ is a member selected from the group consisting of H, C₆-C₁₀ aryl substituted with 6 0-3 R^{1a}, a 5- to 6-membered monocyclic or 8- to 10-membered bicyclic 7 8 heteroaryl containing 1 to 4 heteroatoms each independently a member 9 selected from the group consisting of N, O and S, wherein said heteroaryl is substituted with 0-3 R^{1a}, a C₃-C₈ cycloalkyl substituted with 0-2 R^{1b}, wherein 10 11 said C₃-C₈ cycloalkyl is saturated or unsaturated; and a C₃-C₈ heterocycle 12 containing 1 to 2 heteroatoms each independently a member selected from the 13 group consisting of N, O and S, wherein said heterocycle is substituted with 0-2 R^{1c} and is saturated or unsaturated: 14
- each R^{1a} is independently a member selected from the group consisting of H, C₁-C₃

 perfluoroalkyl, C₃-C₇ cycloalkyl, F, Cl, Br, CN, NO₂, OR¹⁰, SCH₃, S(=O)CH₃,

17	$S(=O)_2R^{10}$, $NR^{11}R^{12}$, acetyl, $C(=O)OR^{13}$, $C(=O)NR^{13}R^{14}$, $S(=O)_2NR^{13}R^{14}$,
18	phenyl substituted with 0-3 R ¹⁵ , a 5- to 6-membered monocyclic heteroaryl
19	containing 1 to 4 heteroatoms each independently a member selected from the
20	group consisting of N, O and S, wherein said heteroaryl is substituted with 0-2
21	R ¹⁵ , a C ₃ -C ₈ heterocycle containing 1 to 2 heteroatoms each independently a
22	member selected from the group consisting of N, O and S, wherein said
23	heterocycle is substituted with 0-2 R1c and is saturated or unsaturated, and a
24	C_1 - C_4 alkyl substituted with 0-2 R^{16} ;
25	each R ^{1b} is independently a member selected from the group consisting of H, OH, F,
26	Cl, acetyl, =O, C_1 - C_6 alkyl, C_1 - C_6 alkoxy, CF_3 and OCF_3 ;
27	each R ^{1c} is independently a member selected from the group consisting of H, OH, F,
28	Cl, =O, C ₁ -C ₆ alkyl substituted with 0-2 R ¹⁶ , C ₁ -C ₆ alkoxy, CF ₃ , OCF ₃ ,
29	C(=O)R ¹⁰ , S(=O) ₂ R ¹⁰ , tBoc, Cbz; phenyl substituted with 0-3 R ¹⁵ ; a 5- to 6-
30	membered monocyclic heteroaryl containing 1 to 4 heteroatoms each
31	independently a member selected from the group consisting of N, O and S,
32	wherein said heteroaryl is substituted with 0-2 R ¹⁵ ;
33	R ² is a member selected from the group consisting of a phenyl substituted with 0-3
34	R ¹⁵ , a 5- to 6-membered monocyclic heteroaryl containing 1 to 4 heteroatoms
35	each independently a member selected from the group consisting of N, O and
36	S, wherein said heteroaryl is substituted with 0-2 R ¹⁵ , a C ₁ -C ₆ alkyl substituted
37	with 0-2 R^{2a} , wherein said C_1 - C_6 alkyl optionally contains a heteroatom
38	selected from the group consisting of $-O$ -, $-S$ -, and $-S(=O)_2$ -, a C_2 - C_6 alkenyl,
39	a C_2 - C_6 alkynyl, a C_3 - C_7 cycloalkyl substituted with 0-2 R^{19} , wherein said C_3 -
40	C ₇ cycloalkyl optionally contains a heteroatom selected from -O-, -S-, and -
41	$S(=O)_2$ -, and a C_7 - C_{11} bicycloalkyl substituted with 0-2 R^{19} ;
42	each R ^{2a} is independently a member selected from the group consisting of a C ₆ -C ₁₀
43	aryl substituted with 0-3 R ¹⁵ , a 5- to 6-membered monocyclic or 8- to 10-
44	membered bicyclic heteroaryl containing 1 to 4 heteroatoms each
45	independently a member selected from the group consisting of N, O and S,
46	wherein said heteroaryl is substituted with 0-3 R ¹⁵ , a C ₃ -C ₈ cycloalkyl
47	substituted with 0-2 R ¹⁹ , and a C ₇ -C ₁₁ bicycloalkyl substituted with 0-2 R ¹⁹ ;
48	R ³ is a member selected from the group consisting of H and C ₁ -C ₄ alkyl;
49	subscript n is 0 or 1;
50	R ⁴ is a member selected from the group consisting of H and C ₁ -C ₆ alkyl;

) [alternatively, K and K are taken together to form a C_5 - C_7 cycloalkyl substituted with
52	0-2 R ¹⁹ ;
53	R ⁵ is a member selected from the group consisting of H, C ₃ -C ₇ cycloalkyl, C ₂ -C ₆
54	alkenyl, C ₂ -C ₆ alkyne, phenyl substituted with 0-2 R ¹⁵ ; 5- to 6-membered
55	heteroaryl containing 1 to 4 heteroatoms each independently a member
56	selected from the group consisting of N, O and S, wherein said heteroaryl is
57	substituted with 0-2 R ¹⁵ , a C ₁ -C ₆ alkyl substituted with 0-2 R ¹⁸ , wherein said
58	C ₁ -C ₆ alkyl optionally contains a heteroatom selected from the group
59	consisting of $-O$ -, $-S$ -, $-S$ ($=O$)-, $-S$ ($=O$) ₂ - and $-NR^{17}$ -;
50	Y is a member independently selected from the group consisting of a bond and
51	$-(CR^{20}R^{21})_{m}-W-(CR^{22}R^{23})_{p}-;$
52	subscript p is 1 or 2;
63	subscript m is 0 or 1;
54	W is a member independently selected from the group consisting of a bond, -O-, -S-,
65	$-S(=O)$ -, $-S(=O)_2$ - and $-NR^{12}$ -;
66	X is selected from the group consisting of -C(=O)-, -OC(=O)-, -NR ²⁴ C(=O)- and
67	$-S(=O)_2-;$
68	each of R ⁶ , R ⁷ , R ⁸ and R ⁹ is independently a member selected from the group
69	consisting of H and C ₁ -C ₄ alkyl;
70	alternatively, R ⁵ and R ⁷ are taken together to form a C ₅ -C ₇ cycloalkyl substituted with
71	0-2 R ¹⁹ ;
72	alternatively, R ⁵ and R ⁹ are taken together to form a 6-7 membered heterocyclic ring
73	containing 1-2 heteroatoms each independently a member selected from the
74	group consisting of N, O and S;
75	Ar is a member selected from the group consisting of phenyl substituted with 0-3 R ²⁹ ,
76	and 5- to 6-membered heteroaryl containing 1 to 4 heteroatoms each
77	independently a member selected from the group consisting of N, O and S,
78	wherein said heteroaryl is substituted with 0-3 R ²⁹ ;
79	each R ¹⁰ is independently a member selected from the group consisting of H, C ₃ -C ₇
80	cycloalkyl, a C_1 - C_3 perfluoroalkyl, a C_1 - C_4 alkyl substituted with 0-1 R^{25} , a
31	phenyl substituted with 0-3 R ¹⁵ ; a 5- to 6-membered heteroaryl containing 1 to
32	4 heteroatoms each independently a member selected from the group
33	consisting of N, O and S, wherein said heteroaryl is substituted with 0-2 R ¹⁵ ,
34	and a C ₃ -C ₈ heterocycle containing 1 to 2 heteroatoms each independently a

85	member selected from the group consisting of N, O and S, wherein said
86	heterocycle is substituted with 0-2 R ^{1c} ;
87	each R ¹¹ is independently a member selected from the group consisting of H, 'BOC,
88	Cbz, C_3 - C_8 cycloalkyl, $(C_1$ - C_6 alkyl)- $C(=O)$ -, $(C_1$ - C_6 alkyl)- $S(=O)_2$ - and a
89	C ₁ -C ₆ alkyl;
90	each of R ¹² , R ¹³ and R ¹⁴ is independently a member selected from the group
91	consisting of H and C ₁ -C ₄ alkyl;
92	alternatively, R^{13} and R^{14} on the same N atom are taken together to form a C_5 - C_7
93	heterocycle containing 1-2 heteroatoms each independently a member selected
94	from the group consisting of N, O and S;
95	each R ¹⁵ is independently a member selected from the group consisting of H, OH, F,
96	Cl, Br, I, CN, NO ₂ , COOR ¹³ , C(=O)NR ¹³ R ¹⁴ , S(=O) ₂ NR ¹³ R ¹⁴ , acetyl, -SCH ₃ ,
97	-S(=O)CH ₃ , -S(=O) ₂ CH ₃ , NR ²⁶ R ²⁷ , C ₁ -C ₆ alkoxy, C ₁ -C ₃ perfluoroalkyl, C ₁ -C ₃
98	perfluoroalkoxy and a C ₁ -C ₆ alkyl;
99	each R ¹⁶ is independently a member selected from the group consisting of H, OH,
100	$COOR^{13}$, $C(=O)NR^{13}R^{14}$, $S(=O)_2NR^{13}R^{14}$, acetyl, $-SCH_3$, $-S(=O)CH_3$,
101	-S(=O) ₂ CH ₃ , C ₁ -C ₆ alkoxy, NR ²⁶ R ²⁷ , a phenyl substituted with 0-3 R ¹⁵ , a 5- to
102	6-membered heteroaryl containing 1 to 4 heteroatoms each independently a
103	member selected from the group consisting of N, O and S, wherein said
104	heteroaryl is substituted with 0-3 R ¹⁵ , and a C ₃ -C ₈ heterocycle containing 1 to
105	2 heteroatoms each independently a member selected from the group
106	consisting of N, O and S, wherein said heterocycle is substituted with 0-2 R ¹⁵
107	and is saturated or unsaturated;
108	R ¹⁷ is a member selected from the group consisting of H and C ₁ -C ₄ alkyl;
109	each R ¹⁸ is independently a member selected from the group consisting of H, OH, F,
110	Cl, CN, NO ₂ , C(=O)OR ³⁰ , C(=O)NR ¹³ R ¹⁴ , NR ¹¹ R ¹² , a C ₁ -C ₃ perfluoroalkyl, a
111	C ₁ -C ₃ perfluoroalkoxy, a phenyl substituted with 0-3 R ¹⁵ , a 5- to 6-membered
112	heteroaryl containing 1 to 4 heteroatoms each independently a member
113	selected from the group consisting of N, O and S, wherein said heteroaryl is
114	substituted with 0-3 R ¹⁵ , a C ₃ -C ₈ heterocycle containing 1 to 2 heteroatoms
115	each independently a member selected from the group consisting of N, O and
116	S, wherein said heterocycle is substituted with 0-2 R ¹⁵ and is saturated or
117	unsaturated; and C ₃ -C ₈ cycloalkyl;

118	each R is a independently a member selected from the group consisting of C_1 - C_4
119	alkyl, F, Cl and C ₁ -C ₄ alkoxy, CF ₃ and OCF ₃ ;
120	alternatively, two R ¹⁹ on the same carbon may be combined to form C ₃ -C ₆ cycloalkyl;
121	each of R^{20} , R^{21} , R^{22} and R^{23} is independently a member selected from the group
122	consisting of a bond, H, F, OH, C ₁ -C ₄ alkyl, and C ₁ -C ₃ alkylhydroxy;
123	alternatively, R^{20} and R^{21} or R^{22} and R^{23} are taken together to form a C_3 - C_6
124	cycloalkyl;
125	R ²⁴ is a member selected from the group consisting of H and C ₁ -C ₄ alkyl;
126	each R ²⁵ is independently a member selected from the group consisting of H, C ₃ -C ₇
127	cycloalkyl, a phenyl substituted with 0-3 R ¹⁵ and a 5- to 6-membered
128	heteroaryl containing 1 to 4 heteroatoms each independently a member
129	selected from the group consisting of N, O and S, wherein said 5- to 6-
130	membered heteroaryl is substituted with 0-2 R ¹⁵ ;
131	each R ²⁶ is independently a member selected from the group consisting of H, C ₁ -C ₄
132	alkyl, $(C_1-C_4 \text{ alkyl})-C(=O)$ - and $(C_1-C_4 \text{ alkyl})-S(=O)_2$ -;
133	each R ²⁷ is independently a member selected from the group consisting of H and
134	C ₁ -C ₄ alkyl;
135	alternatively, R ²⁶ and R ²⁷ on the same N atom are taken together to form a C ₅ -C ₇
136	heterocycle containing 1-2 heteroatoms each independently a member selected
137	from the group consisting of N, O and S;
138	each R ²⁸ is independently a member selected from the group consisting of H, a C ₁ -C ₆
139	alkyl, C ₃ -C ₈ cycloalkyl, a phenyl substituted with 0-3 R ¹⁵ , a benzyl
140	substituted with 0-2 R ¹⁵ ;
141	each R ²⁹ is independently a member selected from the group consisting of H, F, Cl,
142	Br, I, CN, NO ₂ , OR^{28} , SR^{28} , $S(=O)R^{28}$, $S(=O)_2R^{28}$, $S(=O)_2NR^{13}R^{14}$, $NR^{26}R^{27}$,
143	acetyl, $C(=O)NR^{13}R^{14}$, $C(=O)OR^{13}$, C_1-C_6 alkyl, $OCHF_2$, SCF_3 , OCF_3 , -
144	C(=NH)NH ₂ , and 5- to 6-membered heteroaryl containing 1 to 4 heteroatoms
145	each independently a member selected from the group consisting of N, O and
146	S;
147	alternatively, two R ²⁹ substituted on adjacent atoms may be combined to form a 5 to 6
148	membered heterocyclic fused radical, wherein said 5 to 6 membered
149	heterocyclic fused radical comprise 1 or 2 heteroatom(s) selected from O, S
150	and N; wherein said 5 to 6 membered heterocyclic fused radical is substituted
51	with 0-1 oxo;

alternatively, R²⁹ and R⁹ are taken together to form a 5- to 7-membered fused 152 heterocyclic ring containing 1-2 heteroatom(s) each independently a member 153 154 selected from the group consisting of N, O and S; wherein said 5 to 7 membered fused heterocyclic ring is substituted with 0-2 R¹⁹; 155 each R³⁰ is independently a member selected from the group consisting of H, C₃-C₇ 156 cycloalkyl, C₁-C₄ alkyl substituted with 0-1 R²⁵, a phenyl substituted with 0-3 157 R¹⁵, and a 5- to 6-membered heteroaryl containing 1 to 4 heteroatoms each 158 independently a member selected from the group consisting of N, O and S, 159 wherein said heteroaryl is substituted with 0-3 R¹⁵; with the proviso that R³, 160 R⁴, R⁵, R⁶, R⁷, R⁸, and R⁹ are not all hydrogen; and 161 162 an excepient.

- 28. The composition of claim 27, wherein said compound is a member selected from the compounds of Table I.
- 29. A method of selectively inhibiting cathepsin S activity in a mammal in need thereof, comprising administering to said mammal a therapeutically effective amount of a compound of Formula I:

$$R^{1}-Y-X-N-C-[CH]_{n}-H-N-C-C-N-Ar$$

I

or a pharmaceutically acceptable salt or prodrug thereof,

7 wherein:

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R¹ is a member selected from the group consisting of H, C₆-C₁₀ aryl substituted with 8 0-3 R^{1a}, a 5- to 6-membered monocyclic or 8- to 10-membered bicyclic 9 10 heteroaryl containing 1 to 4 heteroatoms each independently a member 11 selected from the group consisting of N, O and S, wherein said heteroarvl is substituted with 0-3 R^{1a}, a C₃-C₈ cycloalkyl substituted with 0-2 R^{1b}, wherein 12 said C₃-C₈ cycloalkyl is saturated or unsaturated; and a C₃-C₈ heterocycle 13 containing 1 to 2 heteroatoms each independently a member selected from the 14 group consisting of N, O and S, wherein said heterocycle is substituted with 15 0-2 R^{1c} and is saturated or unsaturated: 16 each R^{1a} is independently a member selected from the group consisting of H, C₁-C₃ 17

perfluoroalkyl, C₃-C₇ cycloalkyl, F, Cl, Br, CN, NO₂, OR¹⁰, SCH₃, S(=O)CH₃,

19	$S(=O)_2R^{10}$, $NR^{11}R^{12}$, acetyl, $C(=O)OR^{13}$, $C(=O)NR^{13}R^{14}$, $S(=O)_2NR^{13}R^{14}$,
20	phenyl substituted with 0-3 R ¹⁵ , a 5- to 6-membered monocyclic heteroaryl
21	containing 1 to 4 heteroatoms each independently a member selected from the
22	group consisting of N, O and S, wherein said heteroaryl is substituted with 0-2
23	R ¹⁵ , a C ₃ -C ₈ heterocycle containing 1 to 2 heteroatoms each independently a
24	member selected from the group consisting of N, O and S, wherein said
25	heterocycle is substituted with 0-2 R1c and is saturated or unsaturated, and a
26	C ₁ -C ₄ alkyl substituted with 0-2 R ¹⁶ ;
27	each R ^{1b} is independently a member selected from the group consisting of H, OH, F,
28	Cl, acetyl, $=$ O, C ₁ -C ₆ alkyl, C ₁ -C ₆ alkoxy, CF ₃ and OCF ₃ ;
29	each R ^{1c} is independently a member selected from the group consisting of H, OH, F,
30	Cl, =O, C_1 - C_6 alkyl substituted with 0-2 R^{16} , C_1 - C_6 alkoxy, CF_3 , OCF_3 ,
31	C(=O)R ¹⁰ , S(=O) ₂ R ¹⁰ , tBoc, Cbz; phenyl substituted with 0-3 R ¹⁵ ; a 5- to 6-
32	membered monocyclic heteroaryl containing 1 to 4 heteroatoms each
33	independently a member selected from the group consisting of N, O and S,
34	wherein said heteroaryl is substituted with 0-2 R ¹⁵ ;
35	R ² is a member selected from the group consisting of a phenyl substituted with 0-3
36	R ¹⁵ , a 5- to 6-membered monocyclic heteroaryl containing 1 to 4 heteroatoms
37	each independently a member selected from the group consisting of N, O and
38	S, wherein said heteroaryl is substituted with 0-2 R ¹⁵ , a C ₁ -C ₆ alkyl substituted
39	with 0-2 R ^{2a} , wherein said C ₁ -C ₆ alkyl optionally contains a heteroatom
40	selected from the group consisting of -O-, -S-, and -S(=O)2-, a C2-C6 alkenyl,
41	a C_2 - C_6 alkynyl, a C_3 - C_7 cycloalkyl substituted with 0-2 R^{19} , wherein said C_3 -
42	C ₇ cycloalkyl optionally contains a heteroatom selected from -O-, -S-, and -
43	$S(=O)_2$ -, and a C_7 - C_{11} bicycloalkyl substituted with 0-2 R^{19} ;
44	each R ^{2a} is independently a member selected from the group consisting of a C ₆ -C ₁₀
45	aryl substituted with 0-3 R ¹⁵ , a 5- to 6-membered monocyclic or 8- to 10-
46	membered bicyclic heteroaryl containing 1 to 4 heteroatoms each
47	independently a member selected from the group consisting of N, O and S,
48	wherein said heteroaryl is substituted with 0-3 R ¹⁵ , a C ₃ -C ₈ cycloalkyl
49	substituted with 0-2 R ¹⁹ , and a C ₇ -C ₁₁ bicycloalkyl substituted with 0-2 R ¹⁹ ;
50	R ³ is a member selected from the group consisting of H and C ₁ -C ₄ alkyl;
51	subscript n is 0 or 1;
52	R ⁴ is a member selected from the group consisting of H and C ₁ -C ₆ alkyl;

33	alternatively, K and K are taken together to form a C_5 - C_7 cycloalkyl substituted with
54	0-2 R ¹⁹ ;
55	R ⁵ is a member selected from the group consisting of H, C ₃ -C ₇ cycloalkyl, C ₂ -C ₆
56	alkenyl, C ₂ -C ₆ alkyne, phenyl substituted with 0-2 R ¹⁵ ; 5- to 6-membered
57	heteroaryl containing 1 to 4 heteroatoms each independently a member
58	selected from the group consisting of N, O and S, wherein said heteroaryl is
59	substituted with 0-2 R ¹⁵ , a C ₁ -C ₆ alkyl substituted with 0-2 R ¹⁸ , wherein said
60	C ₁ -C ₆ alkyl optionally contains a heteroatom selected from the group
61	consisting of $-O$ -, $-S$ -, $-S$ ($=O$)-, $-S$ ($=O$) ₂ - and $-NR^{17}$ -;
62	Y is a member independently selected from the group consisting of a bond and
63	$-(CR^{20}R^{21})_{m}-W-(CR^{22}R^{23})_{p}-;$
64	subscript p is 1 or 2;
65	subscript m is 0 or 1;
66	W is a member independently selected from the group consisting of a bond, -O-, -S-,
67	$-S(=O)$ -, $-S(=O)_2$ - and $-NR^{12}$ -;
68	X is selected from the group consisting of -C(=O)-, -OC(=O)-, -NR ²⁴ C(=O)- and
69	$-S(=O)_2-;$
70	each of R ⁶ , R ⁷ , R ⁸ and R ⁹ is independently a member selected from the group
71	consisting of H and C ₁ -C ₄ alkyl;
72	alternatively, R ⁵ and R ⁷ are taken together to form a C ₅ -C ₇ cycloalkyl substituted with
73	0-2 R ¹⁹ ;
74	alternatively, R ⁵ and R ⁹ are taken together to form a 6-7 membered heterocyclic ring
75	containing 1-2 heteroatoms each independently a member selected from the
76	group consisting of N, O and S;
7 7	Ar is a member selected from the group consisting of phenyl substituted with 0-3 R ²⁹ ,
78	and 5- to 6-membered heteroaryl containing 1 to 4 heteroatoms each
79	independently a member selected from the group consisting of N, O and S,
80	wherein said heteroaryl is substituted with 0-3 R ²⁹ ;
81	each R ¹⁰ is independently a member selected from the group consisting of H, C ₃ -C ₇
82	cycloalkyl, a C_1 - C_3 perfluoroalkyl, a C_1 - C_4 alkyl substituted with 0-1 \mathbb{R}^{25} , a
83	phenyl substituted with 0-3 R ¹⁵ ; a 5- to 6-membered heteroaryl containing 1 to
84	4 heteroatoms each independently a member selected from the group
85	consisting of N, O and S, wherein said heteroaryl is substituted with 0-2 R ¹⁵ ,
36	and a C ₃ -C ₈ heterocycle containing 1 to 2 heteroatoms each independently a

87	member selected from the group consisting of N, O and S, wherein said
88	heterocycle is substituted with 0-2 R ^{1c} ;
89	each R ¹¹ is independently a member selected from the group consisting of H, 'BOC,
90	Cbz, C_3 - C_8 cycloalkyl, $(C_1$ - C_6 alkyl)- $C(=O)$ -, $(C_1$ - C_6 alkyl)- $S(=O)_2$ - and a
91	C ₁ -C ₆ alkyl;
92	each of R ¹² , R ¹³ and R ¹⁴ is independently a member selected from the group
93	consisting of H and C ₁ -C ₄ alkyl;
94	alternatively, R13 and R14 on the same N atom are taken together to form a C5-C7
95	heterocycle containing 1-2 heteroatoms each independently a member selected
96	from the group consisting of N, O and S;
97	each R ¹⁵ is independently a member selected from the group consisting of H, OH, F,
98	Cl, Br, I, CN, NO ₂ , COOR ¹³ , C(=O)NR ¹³ R ¹⁴ , S(=O) ₂ NR ¹³ R ¹⁴ , acetyl, -SCH ₃ ,
99	-S(=O)CH ₃ , -S(=O) ₂ CH ₃ , NR ²⁶ R ²⁷ , C ₁ -C ₆ alkoxy, C ₁ -C ₃ perfluoroalkyl, C ₁ -C ₃
100	perfluoroalkoxy and a C ₁ -C ₆ alkyl;
101	each R ¹⁶ is independently a member selected from the group consisting of H, OH,
102	$COOR^{13}$, $C(=O)NR^{13}R^{14}$, $S(=O)_2NR^{13}R^{14}$, acetyl, -SCH ₃ , -S(=O)CH ₃ ,
103	-S(=O) ₂ CH ₃ , C ₁ -C ₆ alkoxy, NR ²⁶ R ²⁷ , a phenyl substituted with 0-3 R ¹⁵ , a 5- to
104	6-membered heteroaryl containing 1 to 4 heteroatoms each independently a
105	member selected from the group consisting of N, O and S, wherein said
106	heteroaryl is substituted with 0-3 R ¹⁵ , and a C ₃ -C ₈ heterocycle containing 1 to
107	2 heteroatoms each independently a member selected from the group
108	consisting of N, O and S, wherein said heterocycle is substituted with 0-2 R ¹⁵
109	and is saturated or unsaturated;
110	R ¹⁷ is a member selected from the group consisting of H and C ₁ -C ₄ alkyl;
111	each R ¹⁸ is independently a member selected from the group consisting of H, OH, F,
112	Cl, CN, NO ₂ , C(=O)OR ³⁰ , C(=O)NR ¹³ R ¹⁴ , NR ¹¹ R ¹² , a C_1 - C_3 perfluoroalkyl, a
113	C ₁ -C ₃ perfluoroalkoxy, a phenyl substituted with 0-3 R ¹⁵ , a 5- to 6-membered
114	heteroaryl containing 1 to 4 heteroatoms each independently a member
115	selected from the group consisting of N, O and S, wherein said heteroaryl is
116	substituted with 0-3 R ¹⁵ , a C ₃ -C ₈ heterocycle containing 1 to 2 heteroatoms
117	each independently a member selected from the group consisting of N, O and
118	S, wherein said heterocycle is substituted with 0-2 R ¹⁵ and is saturated or
119	unsaturated; and C ₃ -C ₈ cycloalkyl;

120	each R ¹⁹ is a independently a member selected from the group consisting of C ₁ -C ₄
121	alkyl, F, Cl and C ₁ -C ₄ alkoxy, CF ₃ and OCF ₃ ;
122	alternatively, two R ¹⁹ on the same carbon may be combined to form C ₃ -C ₆ cycloalkyl;
123	each of R ²⁰ , R ²¹ , R ²² and R ²³ is independently a member selected from the group
124	consisting of a bond, H, F, OH, C ₁ -C ₄ alkyl, and C ₁ -C ₃ alkylhydroxy;
125	alternatively, R^{20} and R^{21} or R^{22} and R^{23} are taken together to form a C_3 - C_6
126	cycloalkyl;
127	R ²⁴ is a member selected from the group consisting of H and C ₁ -C ₄ alkyl;
128	each R ²⁵ is independently a member selected from the group consisting of H, C ₃ -C ₇
129	cycloalkyl, a phenyl substituted with 0-3 R ¹⁵ and a 5- to 6-membered
130	heteroaryl containing 1 to 4 heteroatoms each independently a member
131	selected from the group consisting of N, O and S, wherein said 5- to 6-
132	membered heteroaryl is substituted with 0-2 R ¹⁵ ;
133	each R ²⁶ is independently a member selected from the group consisting of H, C ₁ -C ₄
134	alkyl, $(C_1-C_4 \text{ alkyl})-C(=O)$ - and $(C_1-C_4 \text{ alkyl})-S(=O)_2$ -;
135	each R ²⁷ is independently a member selected from the group consisting of H and
136	C_1 - C_4 alkyl;
137	alternatively, R ²⁶ and R ²⁷ on the same N atom are taken together to form a C ₅ -C ₇
138	heterocycle containing 1-2 heteroatoms each independently a member selected
139	from the group consisting of N, O and S;
140	each R ²⁸ is independently a member selected from the group consisting of H, a C ₁ -C ₆
141	alkyl, C_3 - C_8 cycloalkyl, a phenyl substituted with 0-3 \mathbb{R}^{15} , a benzyl
142	substituted with 0-2 R ¹⁵ ;
143	each R ²⁹ is independently a member selected from the group consisting of H, F, Cl,
144	Br, I, CN, NO ₂ , OR^{28} , SR^{28} , $S(=O)R^{28}$, $S(=O)_2R^{28}$, $S(=O)_2NR^{13}R^{14}$, $NR^{26}R^{27}$,
145	acetyl, $C(=O)NR^{13}R^{14}$, $C(=O)OR^{13}$, C_1-C_6 alkyl, $OCHF_2$, SCF_3 , OCF_3 , -
146	C(=NH)NH ₂ , and 5- to 6-membered heteroaryl containing 1 to 4 heteroatoms
147	each independently a member selected from the group consisting of N, O and
148	S;
149	alternatively, two R ²⁹ substituted on adjacent atoms may be combined to form a 5 to 6
150	membered heterocyclic fused radical, wherein said 5 to 6 membered
151	heterocyclic fused radical comprise 1 or 2 heteroatom(s) selected from O, S
152	and N; wherein said 5 to 6 membered heterocyclic fused radical is substituted
153	with 0-1 oxo;

154	alternatively, R ²³ and R ³ are taken together to form a 5- to 7-membered fused
155	heterocyclic ring containing 1-2 heteroatom(s) each independently a member
156	selected from the group consisting of N, O and S; wherein said 5 to 7
157	membered fused heterocyclic ring is substituted with 0-2 R ¹⁹ ;
158	each R ³⁰ is independently a member selected from the group consisting of H, C ₃ -C ₇
159	cycloalkyl, C ₁ -C ₄ alkyl substituted with 0-1 R ²⁵ , a phenyl substituted with 0-3
160	R ¹⁵ , and a 5- to 6-membered heteroaryl containing 1 to 4 heteroatoms each
161	independently a member selected from the group consisting of N, O and S,
162	wherein said heteroaryl is substituted with 0-3 R ¹⁵ ; and
163	with the proviso that R ³ , R ⁴ , R ⁵ , R ⁶ , R ⁷ , R ⁸ , and R ⁹ are not all hydrogen.
1	30. The method of claim 29, wherein the cathepsin S inhibition constant
2	for a compound of Formula I is less than 10 μM .
1	31. The method of claim 30, wherein the cathepsin S inhibition constant
2	for a compound of Formula I is less than 1.0 μM .
1	32. The method of claim 31, wherein the cathepsin S inhibition constant
2	for a compound of Formula I is less than 0.1 μM.
1	33. The method of claim 29, wherein cathepsin S is selectively inhibited in
2	the presence of at least one other cathepsin.
1	34. The method of claim 33, wherein the inhibition constant of a
2	compound of Formula I for said at least one other cathepsin is at least 10 times greater than a
3	cathepsin S inhibition constant of a compound of Formula I.
1	35. The method of claim 34, wherein the inhibition constant of a
2	compound of Formula I for said at least one other cathepsin is at least 100 times greater than
3	said cathepsin S inhibition constant of a compound of Formula I.
1	36. The method of claim 35, wherein the inhibition constant of a
2	compound of Formula I for said at least one other cathepsin is at least 1000 times greater than
3	said cathensin S inhibition constant of a compound of Formula I

- 1 37. The method of claim 29, wherein said compound is a member selected
- 2 from the compounds of Table I.